

characterize the protein. A starting material that can only be used to produce a final product does not have a substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving the claimed cDNA have asserted or identified specific and substantial utilities. The research contemplated by Applicants to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of the protein itself or the mechanisms in which the protein is involved does not define a "real world" context of use. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the cDNA compounds such that another non-asserted utility would be well established for the compounds.

Claim 1 is also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

**Example 10: DNA Fragment encoding a Full Open Reading Frame (ORF)**

**Specification:** The specification discloses that a cDNA library was prepared from human kidney epithelial cells and 5000 members of this library were

sequenced and open reading frames were identified. The specification discloses a Table that indicates that one member of the library having SEQ ID NO: 2 has a high level of homology to a DNA ligase. The specification teaches that this complete ORF (SEQ ID NO: 2) encodes SEQ ID NO: 3. An alignment of SEQ ID NO: 3 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO: 3 and the consensus sequence of the known DNA ligases that are presented in the specification reveals a similarity score of 95%. A search of the prior art confirms that SEQ ID NO: 2 has high homology to DNA Ligase encoding nucleic acids and that the next highest level of homology is to alpha-actin. However, the latter homology is only 50%. Based on the sequence homologies, the specification asserts that SEQ ID NO: 2 encodes a DNA ligase.

**Claim 1:** An isolated and purified nucleic acid comprising SEQ ID NO: 2.

**Analysis:** The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts:

1) Based on the record, is there a "well established utility" for the claimed invention? Based upon applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO: 2 encodes a DNA ligase. Further, DNA ligases have a well-established use in the molecular biology art based on this class of protein's ability to ligate DNA. Consequently the answer to the question is yes.

Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed. In order to determine whether the claimed invention has a well-established utility the examiner must determine that the invention has a specific, substantial and credible utility that would have been readily apparent to one of skill in the art. In this case SEQ ID NO: 2 was shown to encode a DNA ligase that the artisan would have recognized as having a specific, substantial and credible utility based on its enzymatic activity.

Thus, the conclusion reached from this analysis is that a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should not be made.

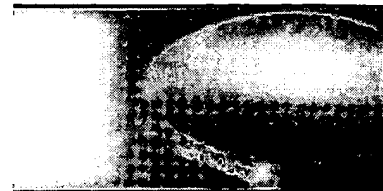
**Example 11: Animals with Uncharacterized Human Genes**

**Specification:** Kidney cells from a patient with Polycystic Kidney (PCK) Disease have been used to make a cDNA library. From this library 8000 nucleotide "fragments" have been sequenced but not yet used to express proteins in a transformed host cell nor have they been characterized in any other way. The 50 longest fragments, SEQ ID NO: 1-50, respectively, have been used to make transgenic mice. None of the 50 lines of mice have developed Polycystic Kidney Disease to date. The asserted utility is the use of the mice to research human genes from diseased human kidneys. The disease is inheritable, but chromosomal loci have not yet been identified. Neither the absence or presence of a specific protein has been identified with the disease condition.

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## Institut für Pharmakologie und Toxikologie

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Prof. Dr. Ernst Petzinger

**Petzinger, E., Ziegler, K.**

Ochratoxin A from a toxicological perspective.  
J. vet. Pharmacol. Therap. 23: 91-98, 2000

**Honscha W., Dötsch K.U., Thomsen, N., Petzinger, E.**

Cloning and functional characterization of the bile acid sensitive methotrexate carrier fr  
liver cells.  
Hepatology 31: 1296-1304, 2000

**Starke, D., Lischka, K., Pagels, P., Uhlmann, E., Kramer, W., Wess, G., Petzinger, E.**

Bile acid - oligodeoxynucleotide conjugates: Synthesis and liver excretion in rats.  
Biorg. Medicin. Chem. Lett. 11: 945-949, 2001

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Mycotox. Res. 16A, 189-193, 2001

**Geyer, J., Petzinger, E.**

Cloning of a new member of the OATP family from bovine liver.  
Accession number AY052775 from 28-Aug-2001; Complete sequence.  
NCBI-GenBank, NIH Bethesda, MD 20894, USA

**Geyer, J., Petzinger, E.**

Cloning of a new member of the OATP- family from bovine kidney (homolog of OATP-A)  
Accession number AJ508718.1 from 23-Sep-2002; OATP-A gene; Complete sequence.  
EMBL/GenBank/DDBJ databases. NCBI NM\_174654; locus SLC21A3.

**Doering, B., Geyer, J., Petzinger, E.**

Cloning of a new member of the OATP family from bovine liver (homolog of OATP-C)  
Accession number AJ508747 from 23-Sep-2002; OATP-C gene; Complete sequence  
EMBL/GenBank/DDBJ databases

**Geyer, J., Petzinger, E.**

Cloning of a new member of the OATP-family from bovine kidney (homolog of OATP-D)  
Accession number AJ508719 from 23-Sep-2002; OATP-D gene; Complete sequence  
EMBL/GenBank/DDBJ databases

**Geyer, J., Petzinger, E.**

*Cloning of a new member of the OATP family from bovine brain (homolog of OATP-B)  
Accession number AJ534982.1 from 13-Dec-2002; OATP-B gene; Complete sequence  
EMBL/GenBank/DDBJ databases. NCBI NM\_174843; locus SLC21A9*

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**Geyer, J., Petzinger, E.**

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**Petzinger, E.**

From transport studies to drugs: Liver-targeting with bile acids. What we have learned  
outlook on oligodeoxynucleotides.  
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**Zahner, D., Eckhardt, U., Petzinger, E.**

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Biochemical Pharmacology, 66; 565-577, 2003

**Weidenbach, A. Petzinger, E.**

Ochratoxin A: Toxicology of an abundant mycotoxin  
Research Trends, in press 2003

**Geyer, J., Petzinger, E.**

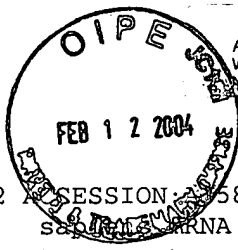
*Cloning of the organic anion transporter 1 from bovine kidney.  
Accession number AJ549816.1 from 12. March 2003, Oat1 gene;  
EMBL/GenBank/DDBJ databases*

---

**Historische Publikationen**

Petzinger, E. (1984) Die Bedeutung des Gallensäuretransportes für die Aufna  
Fremdstoffen in Leberparenchymzellen. Habilitationsschrift, Justus-Liebig-Universität, G

Petzinger, E. (1994) Transport of organic anions in the liver. An update on bile acid, f  
monocarboxylate, anionic amino acid, cholephilic organic anion, and anionic drug trans  
Physiol. Biochem. Pharmacol. 123: 41-201



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Length = 1134

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Identities = 377/377 (100%), Positives = 377/377 (100%)  
Frame = +1

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☐ 1: [AJ583502](#). Homo sapiens mRNA...[gi:35208820]

Links

LOCUS AJ583502 1134 bp mRNA linear PRI 24-SEP-2003  
DEFINITION Homo sapiens mRNA for sodium-dependent organic anion transporter (SOAT gene).

ACCESSION AJ583502

VERSION AJ583502.1 GI:35208820

KEYWORDS SOAT gene; sodium-dependent organic anion transporter.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1

AUTHORS Geyer, J. and Petzinger, E.

TITLE cloning of a sodium-dependent organic anion transporter (SOAT) from human adrenal gland

JOURNAL Unpublished

REFERENCE 2 (bases 1 to 1134)

AUTHORS Geyer, J.

TITLE Direct Submission

JOURNAL Submitted (23-SEP-2003) Geyer J., Institute of Pharmacology and Toxicology, University of Giessen, Frankfurter Str. 107, 35392 Giessen, GERMANY

FEATURES

Location/Qualifiers

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Jan 29 2004 15:38:25



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 (1134 letters)

Sequences producing significant alignments:	Score (bits)	E Value
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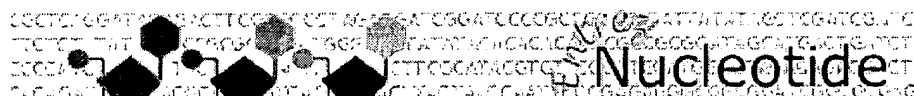
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☐ 1: AC079237. Homo sapiens BAC ...[gi:18482358] [Links](#)

LOCUS AC079237 23618 bp DNA linear PRI 21-FEB-2002

DEFINITION Homo sapiens BAC clone RP11-711J3 from 4, complete sequence.

ACCESSION AC079237

VERSION AC079237.7 GI:18482358

KEYWORDS HTG.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 23618)

AUTHORS Sulston, J.E. and Waterston, R.

TITLE Toward a complete human genome sequence

JOURNAL Genome Res. 8 (11), 1097-1108 (1998)

MEDLINE 99063792

PUBMED 9847074

REFERENCE 2 (bases 1 to 23618)

AUTHORS Radionenko, M. and Meyer, R.

TITLE The sequence of Homo sapiens BAC clone RP11-711J3

JOURNAL Unpublished (2001)

REFERENCE 3 (bases 1 to 23618)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (24-AUG-2000) Genome Sequencing Center, Washington  
University School of Medicine, 4444 Forest Park Parkway, St. Louis,  
MO 63108, USA

REFERENCE 4 (bases 1 to 23618)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (03-FEB-2002) Genome Sequencing Center, Washington  
University School of Medicine, 4444 Forest Park Parkway, St. Louis,  
MO 63108, USA

REFERENCE 5 (bases 1 to 23618)

AUTHORS Waterston, R.

TITLE Direct Submission

JOURNAL Submitted (21-FEB-2002) Department of Genetics, Washington  
University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA

COMMENT On Feb 3, 2002 this sequence version replaced gi:18151062.

----- Genome Center

Center: Washington University Genome Sequencing Center

Center code: WUGSC

Web site: <http://genome.wustl.edu/gsc>

Contact: [sapiens@watson.wustl.edu](mailto:sapiens@watson.wustl.edu)

----- Summary Statistics

Center project name: H\_NH0711J03

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NOTICE: This sequence may not represent the entire insert of this clone. It may be shorter because we only sequence overlapping



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☐ 1: AC105413. Homo sapiens BAC ...[gi:18464262]

Links

LOCUS AC105413 65958 bp DNA linear PRI 21-FEB-2002

DEFINITION Homo sapiens BAC clone RP11-64A1 from 4, complete sequence.

ACCESSION AC105413 AC007525

VERSION AC105413.3 GI:18464262

KEYWORDS HTG.

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ORGANISM Homo sapiens  
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 65958)

AUTHORS Sulston, J.E. and Waterston, R.

TITLE Toward a complete human genome sequence

JOURNAL Genome Res. 8 (11), 1097-1108 (1998)

MEDLINE 99063792

PUBMED 9847074

REFERENCE 2 (bases 1 to 65958)

AUTHORS Isak, A. and Cotton, M.

TITLE The sequence of Homo sapiens BAC clone RP11-64A1

JOURNAL Unpublished (2001)

REFERENCE 3 (bases 1 to 65958)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (04-JAN-2002) Genome Sequencing Center, Washington  
University School of Medicine, 4444 Forest Park Parkway, St. Louis,  
MO 63108, USA

REFERENCE 4 (bases 1 to 65958)

AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (01-FEB-2002) Genome Sequencing Center, Washington  
University School of Medicine, 4444 Forest Park Parkway, St. Louis,  
MO 63108, USA

REFERENCE 5 (bases 1 to 65958)

AUTHORS Waterston, R.

TITLE Direct Submission

JOURNAL Submitted (21-FEB-2002) Department of Genetics, Washington  
University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA

COMMENT On Feb 1, 2002 this sequence version replaced gi:18151029.

----- Genome Center

Center: Washington University Genome Sequencing Center

Center code: WUGSC

Web site: <http://genome.wustl.edu/gsc>Contact: [sapiens@watson.wustl.edu](mailto:sapiens@watson.wustl.edu)

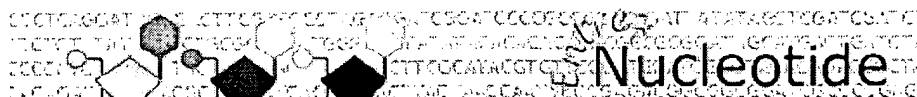
----- Summary Statistics

Center project name: H\_NH0064A01

Drafting Center: WIBR

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NOTICE: This sequence may not represent the entire insert of this



Entrez PubMed Nucleotide Protein Genome Structure PMC Taxonomy Books

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☐ 1: NM\_008337. Mus musculus inte...[gi:33468858] [Links](#)

LOCUS NM\_008337 1208 bp mRNA linear ROD 20-DEC-2003

DEFINITION Mus musculus interferon gamma (Ifng), mRNA.

ACCESSION NM\_008337

VERSION NM\_008337.1 GI:33468858

KEYWORDS

SOURCE Mus musculus (house mouse)

ORGANISM Mus musculus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.

REFERENCE 1 (bases 1 to 1208)

AUTHORS Liu,J., Cao,S., Herman,L.M. and Ma,X.

TITLE Differential regulation of interleukin (IL)-12 p35 and p40 gene expression and interferon (IFN)-gamma-primed IL-12 production by IFN regulatory factor 1

JOURNAL J. Exp. Med. 198 (8), 1265-1276 (2003)

PUBMED 14568984

REFERENCE 2 (bases 1 to 1208)

AUTHORS Matthys,P., Lories,R.J., De Klerck,B., Heremans,H., Luyten,F.P. and Billiau,A.

TITLE Dependence on interferon-gamma for the spontaneous occurrence of arthritis in DBA/1 mice

JOURNAL Arthritis Rheum. 48 (10), 2983-2988 (2003)

PUBMED 14558106

REMARK GeneRIF: endogenous IFNgamma plays an important role in the initial stages of spontaneous arthritis, and that the inflammatory components in its pathogenesis are more prominent than has been believed.

REFERENCE 3 (bases 1 to 1208)

AUTHORS Biondo,C., Beninati,C., Bombaci,M., Messina,L., Mancuso,G., Midiri,A., Galbo,R. and Teti,G.

TITLE Induction of T helper type 1 responses by a polysaccharide deacetylase from Cryptococcus neoformans

JOURNAL Infect. Immun. 71 (9), 5412-5417 (2003)

PUBMED 12933895

REMARK GeneRIF: A 25-kDa cryptococcal deacetylase (d25) was found to induce secretion of interleukin 2 and gamma interferon in spleen cells from d25-immunized or Cryptococcus neoformans-infected mice.

REFERENCE 4 (bases 1 to 1208)

AUTHORS McLoughlin,R.M., Witowski,J., Robson,R.L., Wilkinson,T.S., Hurst,S.M., Williams,A.S., Williams,J.D., Rose-John,S., Jones,S.A. and Topley,N.

TITLE Interplay between IFN-gamma and IL-6 signaling governs neutrophil trafficking and apoptosis during acute inflammation

JOURNAL J. Clin. Invest. 112 (4), 598-607 (2003)

PUBMED 12925700

REMARK GeneRIF: IFN-gamma has a pivotal role in regulating innate immunity through control of both the recruitment and clearance phases of neutrophil trafficking

- REFERENCE 5 (bases 1 to 1208)  
AUTHORS Wang,J., Pham-Mitchell,N., Schindler,C. and Campbell,I.L.  
TITLE Dysregulated Sonic hedgehog signaling and medulloblastoma consequent to IFN-alpha-stimulated STAT2-independent production of IFN-gamma in the brain  
JOURNAL J. Clin. Invest. 112 (4), 535-543 (2003)  
PUBMED [12925694](#)  
REMARK GeneRIF: IFNg regulates sonic hedgehog signaling in the central nervous system
- REFERENCE 6 (bases 1 to 1208)  
AUTHORS Ain,R., Canham,L.N. and Soares,M.J.  
TITLE Gestation stage-dependent intrauterine trophoblast cell invasion in the rat and mouse: novel endocrine phenotype and regulation  
JOURNAL Dev. Biol. 260 (1), 176-190 (2003)  
PUBMED [12885563](#)  
REMARK GeneRIF: Ifng inhibits trophoblast cell outgrowth, and trophoblast cell invasion is accelerated in mice with a genetic deficiency in the Ifng.
- REFERENCE 7 (bases 1 to 1208)  
AUTHORS Nabbe,K.C., van Lent,P.L., Holthuysen,A.E., Kolls,J.K., Verbeek,S. and van den Berg,W.B.  
TITLE FcgammaRI up-regulation induced by local adenoviral-mediated interferon-gamma production aggravates chondrocyte death during immune complex-mediated arthritis  
JOURNAL Am. J. Pathol. 163 (2), 743-752 (2003)  
PUBMED [12875993](#)  
REMARK GeneRIF: These results indicate that interferon-gamma overexpression enhances cartilage destruction in the presence of immune complexes and that FcgammaRI is crucial in the development of chondrocyte death.
- REFERENCE 8 (bases 1 to 1208)  
AUTHORS Souto,J.T., Aliberti,J.C., Campanelli,A.P., Livonesi,M.C., Maffei,C.M., Ferreira,B.R., Travassos,L.R., Martinez,R., Rossi,M.A. and Silva,J.S.  
TITLE Chemokine production and leukocyte recruitment to the lungs of Paracoccidioides brasiliensis-infected mice is modulated by interferon-gamma  
JOURNAL Am. J. Pathol. 163 (2), 583-590 (2003)  
PUBMED [12875978](#)  
REMARK GeneRIF: results suggest that IFN-gamma modulates the expression of chemokines and chemokine receptors as well as the kind of cells that infiltrate the lungs of Paracoccidioides brasiliensis-infected mice
- REFERENCE 9 (bases 1 to 1208)  
AUTHORS Hogan,J.C. and Stephens,J.M.  
TITLE STAT 1 binds to the LPL promoter in vitro  
JOURNAL Biochem. Biophys. Res. Commun. 307 (2), 350-354 (2003)  
PUBMED [12859963](#)  
REMARK GeneRIF: Results identify a STAT1 binding site within the murine lipoprotein lipase (LPL) promoter which likely plays a role in the interferon-gamma-induced decrease of LPL expression.
- REFERENCE 10 (bases 1 to 1208)  
AUTHORS Delgado,M.  
TITLE Inhibition of interferon (IFN) gamma-induced Jak-STAT1 activation in microglia by vasoactive intestinal peptide: inhibitory effect on CD40, IFN-induced protein-10, and inducible nitric-oxide synthase expression  
JOURNAL J. Biol. Chem. 278 (30), 27620-27629 (2003)  
PUBMED [12754213](#)  
REMARK GeneRIF: down-regulation of IFN-gamma-induced gene expression by

VIP and PACAP is important for regulation of the inflammatory response in the central nervous system

REFERENCE 11 (bases 1 to 1208)

AUTHORS Lugo-Villarino,G., Maldonado-Lopez,R., Possemato,R., Penaranda,C. and Glimcher,L.H.

TITLE T-bet is required for optimal production of IFN-gamma and antigen-specific T cell activation by dendritic cells

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 100 (13), 7749-7754 (2003)

PUBMED [12802010](#)

REMARK GenerIF: interferon gamma production requires T-bet

REFERENCE 12 (bases 1 to 1208)

AUTHORS Barin,J.G., Afanasyeva,M., Talor,M.V., Rose,N.R., Burek,C.L. and Caturegli,P.

TITLE Thyroid-specific expression of IFN-gamma limits experimental autoimmune thyroiditis by suppressing lymphocyte activation in cervical lymph nodes

JOURNAL J. Immunol. 170 (11), 5523-5529 (2003)

PUBMED [12759429](#)

REMARK GenerIF: This study supports a disease-limiting role of IFN-gamma in experimental autoimmune thyroiditis and provides the first evidence that local IFN-gamma activity in the thyroid is sufficient for disease suppression.

REFERENCE 13 (bases 1 to 1208)

AUTHORS Mead,J.R., Hughes,T.R., Irvine,S.A., Singh,N.N. and Ramji,D.P.

TITLE Interferon-gamma stimulates the expression of the inducible cAMP early repressor in macrophages through the activation of casein kinase 2. A potentially novel pathway for interferon-gamma-mediated inhibition of gene transcription

JOURNAL J. Biol. Chem. 278 (20), 17741-17751 (2003)

PUBMED [12609974](#)

REMARK GenerIF: Interferon-gamma stimulates the expression of the inducible cAMP early repressor in macrophages through the activation of casein kinase 2

REFERENCE 14 (bases 1 to 1208)

AUTHORS Watanabe,Y., Suzuki,O., Haruyama,T. and Akaike,T.

TITLE Interferon-gamma induces reactive oxygen species and endoplasmic reticulum stress at the hepatic apoptosis

JOURNAL J. Cell. Biochem. 89 (2), 244-253 (2003)

PUBMED [12704788](#)

REMARK GenerIF: role in inducing reactive oxygen species and endoplasmic reticulum stress at the hepatic apoptosis

REFERENCE 15 (bases 1 to 1208)

AUTHORS Enzler,T., Gillessen,S., Manis,J.P., Ferguson,D., Fleming,J., Alt,F.W., Mihm,M. and Dranoff,G.

TITLE Deficiencies of GM-CSF and interferon gamma link inflammation and cancer

JOURNAL J. Exp. Med. 197 (9), 1213-1219 (2003)

PUBMED [12732663](#)

REMARK GenerIF: role of deficiency in linking inflammation and cancer

REFERENCE 16 (bases 1 to 1208)

AUTHORS Stokes,K.Y., Clanton,E.C., Clements,K.P. and Granger,D.N.

TITLE Role of interferon-gamma in hypercholesterolemia-induced leukocyte-endothelial cell adhesion

JOURNAL Circulation 107 (16), 2140-2145 (2003)

PUBMED [12695304](#)

REMARK GenerIF: Interferon-gamma has a role in hypercholesterolemia-induced leukocyte-endothelial cell adhesion.

REFERENCE 17 (bases 1 to 1208)

AUTHORS Singh,N.P., Guo,L., Mhoyan,A. and Shirwan,H.

TITLE Predominant expression of Th2 cytokines and interferon-gamma in



xenogeneic cardiac grafts undergoing acute vascular rejection  
JOURNAL Transplantation 75 (5), 586-590 (2003)  
PUBMED [12640294](#)  
REMARK GeneRIF: Predominant expression of Th2 cytokines and IFN-gamma in cardiac xenografts undergoing acute vascular rejection.

REFERENCE 18 (bases 1 to 1208)  
AUTHORS Mullins,D.W., Martins,R.S. and Elgert,K.D.  
TITLE Tumor-derived cytokines dysregulate macrophage interferon-gamma responsiveness and interferon regulatory factor-8 expression  
JOURNAL Exp. Biol. Med. (Maywood) 228 (3), 270-277 (2003)  
PUBMED [12626771](#)  
REMARK GeneRIF: dysregulation by tumor-derived cytokines

REFERENCE 19 (bases 1 to 1208)  
AUTHORS Bergmann,C.C., Parra,B., Hinton,D.R., Chandran,R., Morrison,M. and Stohlman,S.A.  
TITLE Perforin-mediated effector function within the central nervous system requires IFN-gamma-mediated MHC up-regulation  
JOURNAL J. Immunol. 170 (6), 3204-3213 (2003)  
PUBMED [12626579](#)  
REMARK GeneRIF: IFN-gamma secretion by CD8+ T cells is critical for viral clearance and up-regulation of MHC expression in brains and spinal cords of mice infected with the JHM strain of mouse hepatitis virus.

REFERENCE 20 (bases 1 to 1208)  
AUTHORS Buono,C., Come,C.E., Stavrakis,G., Maguire,G.F., Connelly,P.W. and Lichtman,A.H.  
TITLE Influence of interferon-gamma on the extent and phenotype of diet-induced atherosclerosis in the LDLR-deficient mouse  
JOURNAL Arterioscler. Thromb. Vasc. Biol. 23 (3), 454-460 (2003)  
PUBMED [12615659](#)  
REMARK GeneRIF: These data provide direct evidence that IFN-gamma influences atherosclerosis development and phenotype in the LDLR-deficient mouse, independent of changes in blood lipoprotein profiles.

REFERENCE 21 (bases 1 to 1208)  
AUTHORS Hort,G.M., Weisenburger,J., Borsdorf,B., Peters,C., Banai,M., Hahn,H., Jacob,J. and Mielke,M.E.  
TITLE Delayed type hypersensitivity-associated disruption of splenic periarteriolar lymphatic sheaths coincides with temporary loss of IFN-gamma production and impaired eradication of bacteria in Brucella abortus-infected mice  
JOURNAL Microbes Infect. 5 (2), 95-106 (2003)  
PUBMED [12650767](#)  
REMARK GeneRIF: severe disruption of spleen morphology during Brucella abortus induced delayed type hypersensitivity results in an impaired capacity of splenocytes to produce IFN-gamma in response to soluble Brucella antigen

REFERENCE 22 (bases 1 to 1208)  
AUTHORS Shi,M., Pan,W. and Tabel,H.  
TITLE Experimental African trypanosomiasis: IFN-gamma mediates early mortality  
JOURNAL Eur. J. Immunol. 33 (1), 108-118 (2003)  
PUBMED [12594839](#)  
REMARK GeneRIF: Experimental African trypanosomiasis: IFN-gamma mediates early mortality

REFERENCE 23 (bases 1 to 1208)  
AUTHORS Hayashi,H., Inoue,Y., Tsutsui,H., Okamura,H., Nakanishi,K. and Onozaki,K.  
TITLE TGFbeta down-regulates IFN-gamma production in IL-18 treated NK cell line LNK5E6

JOURNAL Biochem. Biophys. Res. Commun. 300 (4), 980-985 (2003)  
PUBMED [12559970](#)  
REMARK GeneRIF: Results suggest that the destabilization of interferon-gamma (IFN-gamma) mRNA induced by transforming growth factor beta leads to the inhibition of antiviral activity and IFN-gamma production in interleukin-18-stimulated LNK5E6 cells.

REFERENCE 24 (bases 1 to 1208)  
AUTHORS Purdy,A., Case,L., Duvall,M., Overstrom-Coleman,M., Monnier,N., Chervonsky,A. and Golovkina,T.  
TITLE Unique resistance of I/LnJ mice to a retrovirus is due to sustained interferon gamma-dependent production of virus-neutralizing antibodies

JOURNAL J. Exp. Med. 197 (2), 233-243 (2003)  
PUBMED [12538662](#)  
REMARK GeneRIF: Resistance to MMTV infection was recessive and was dependent on interferon (IFN)-gamma production.

REFERENCE 25 (bases 1 to 1208)  
AUTHORS Mackler,A.M., Barber,E.M., Takikawa,O. and Pollard,J.W.  
TITLE Indoleamine 2,3-dioxygenase is regulated by IFN-gamma in the mouse placenta during *Listeria monocytogenes* infection

JOURNAL J. Immunol. 170 (2), 823-830 (2003)  
PUBMED [12517946](#)  
REMARK GeneRIF: During *Listeria monocytogenes* infection, IFN-gamma regulates the expression of indoleamine 2,3-dioxygenase in the placenta.

REFERENCE 26 (bases 1 to 1208)  
AUTHORS Delneste,Y., Charbonnier,P., Herbault,N., Magistrelli,G., Caron,G., Bonnefoy,J.Y. and Jeannin,P.  
TITLE Interferon-gamma switches monocyte differentiation from dendritic cells to macrophages

JOURNAL Blood 101 (1), 143-150 (2003)  
PUBMED [12393446](#)  
REMARK GeneRIF: IFN-gamma skews murine bone marrow progenitor differentiation from dendritic cells to macrophagelike cells.

REFERENCE 27 (bases 1 to 1208)  
AUTHORS Perales,M.A., Fantuzzi,G., Goldberg,S.M., Turk,M.J., Mortazavi,F., Busam,K., Houghton,A.N., Dinarello,C.A. and Wolchok,J.D.  
TITLE GM-CSF DNA induces specific patterns of cytokines and chemokines in the skin: implications for DNA vaccines

JOURNAL Cytokines Cell Mol Ther 7 (3), 125-133 (2002)  
PUBMED [12850812](#)  
REMARK GeneRIF: Gm-Csf induced high levels of Ifng.

REFERENCE 28 (bases 1 to 1208)  
AUTHORS Rodrigues,E.G. and Travassos,L.R.  
TITLE Endogenous accumulation of IFN-gamma in IFN-gamma-R(-/-) mice increases resistance to B16F10-Nex2 murine melanoma: a model for direct IFN-gamma anti-tumor cytotoxicity in vitro and in vivo

JOURNAL Cytokines Cell Mol Ther 7 (3), 107-116 (2002)  
PUBMED [12850810](#)  
REMARK GeneRIF: Endogenous accumulation of Ifng in Ifng-R (-/-) mice increases resistance to B16F10-Nex2 murine melanoma.

REFERENCE 29 (bases 1 to 1208)  
AUTHORS Sewnath,M.E., Van Der Poll,T., Van Noorden,C.J., Ten Kate,F.J. and Gouma,D.J.  
TITLE Endogenous interferon gamma protects against cholestatic liver injury in mice

JOURNAL Hepatology 36 (6), 1466-1477 (2002)  
PUBMED [12447873](#)  
REMARK GeneRIF: IFN-gamma protects against liver injury during extrahepatic cholestasis by stimulation of apoptosis and subsequent

- proliferation of hepatocytes, leading to elegant removal of damaged hepatocytes, thus preventing necrosis and inflammatory responses.
- REFERENCE 30 (bases 1 to 1208)  
AUTHORS Lewkowich, I.P. and HayGlass, K.T.  
TITLE Endogenous IFN-gamma and IL-18 production directly limit induction of type 2 immunity in vivo  
JOURNAL Eur. J. Immunol. 32 (12), 3536-3545 (2002)  
PUBMED [12442336](#)  
REMARK GenerIF: endogenous IFN-gamma and IL-18 are potent, independent, negative regulators of the development of type 2 immunity to ubiquitous environmental antigens
- REFERENCE 31 (bases 1 to 1208)  
AUTHORS McCartney-Francis, N.L. and Wahl, S.M.  
TITLE Dysregulation of IFN-gamma signaling pathways in the absence of TGF-beta 1  
JOURNAL J. Immunol. 169 (10), 5941-5947 (2002)  
PUBMED [12421979](#)  
REMARK GenerIF: Coincident up-regulation of IFN-gamma and inducible nitric oxide synthase before the appearance of inflammation suggests that failed regulation of the IFN-gamma signaling pathway may underlie the immunological disorder in TGF-beta 1 null mice.
- REFERENCE 32 (bases 1 to 1208)  
AUTHORS Andoh, A., Masuda, A., Kumazawa, Y. and Kasajima, T.  
TITLE Serum antibody response and nasal lymphoid tissue (NALT) structure in the absence of IL-4 or IFN-gamma  
JOURNAL Cytokine 20 (3), 107-112 (2002)  
PUBMED [12453468](#)  
REMARK GenerIF: serum antibody responses and nasal lymphoid tissue structures in interleukin (IL)-4 gene targeted (IL-4(-/-)) and interferon (IFN)-gamma gene targeted (IFN-gamma(-/-)) mice
- REFERENCE 33 (bases 1 to 1208)  
AUTHORS Pal, E. and Tabira, T.  
TITLE Autonomic regulation of experimental autoimmune encephalomyelitis: the role of interferon-gamma  
JOURNAL Neuroimmunomodulation 10 (2), 80-84 (2002)  
PUBMED [12372981](#)  
REMARK GenerIF: that control of actively induced experimental autoimmune encephalomyelitis by the sympathetic nervous system depends on INF-gamma and the integrity of the cytokine network.
- REFERENCE 34 (bases 1 to 1208)  
AUTHORS Woo, A.L., Gildea, L.A., Tack, L.M., Miller, M.L., Spicer, Z., Millhorn, D.E., Finkelman, F.D., Hassett, D.J. and Shull, G.E.  
TITLE In vivo evidence for interferon-gamma-mediated homeostatic mechanisms in small intestine of the NHE3 Na<sup>+</sup>/H<sup>+</sup> exchanger knockout model of congenital diarrhea  
JOURNAL J. Biol. Chem. 277 (50), 49036-49046 (2002)  
PUBMED [12370192](#)  
REMARK GenerIF: elevated interferon-gamma, produced by gut-associated lymphoid tissue in the small intestine, is part of a homeostatic mechanism that is activated in response to the intestinal absorptive defect in order to regulate the fluidity of the intestinal tract
- REFERENCE 35 (bases 1 to 1208)  
AUTHORS Kuwata, T., Gongora, C., Kanno, Y., Sakaguchi, K., Tamura, T., Kanno, T., Basrur, V., Martinez, R., Appella, E., Golub, T. and Ozato, K.  
TITLE Gamma interferon triggers interaction between ICSBP (IRF-8) and TEL, recruiting the histone deacetylase HDAC3 to the interferon-responsive element  
JOURNAL Mol. Cell. Biol. 22 (21), 7439-7448 (2002)  
PUBMED [12370291](#)

REMARK      GenerIF: interferon gamma is required for the binding between IRF-8 and TEL that recruits HDAC3

REFERENCE    36 (bases 1 to 1208)

AUTHORS      Horton,M.R., Boodoo,S. and Powell,J.D.

TITLE        NF-kappa B activation mediates the cross-talk between extracellular matrix and interferon-gamma (IFN-gamma) leading to enhanced monokine induced by IFN-gamma (MIG) expression in macrophages

JOURNAL      J. Biol. Chem. 277 (46), 43757-43762 (2002)

PUBMED       [12226082](#)

REMARK      GenerIF: NF-kappaB has a critical role in mediating IFN-gamma-induced MIG (monokine induced by IFN-gamma) expression independent of hyaluronan

REFERENCE    37 (bases 1 to 1208)

AUTHORS      Ami,K., Kinoshita,M., Yamauchi,A., Nishikage,T., Habu,Y., Shinomiya,N., Iwai,T., Hiraide,H. and Seki,S.

TITLE        IFN-gamma production from liver mononuclear cells of mice in burn injury as well as in postburn bacterial infection models and the therapeutic effect of IL-18

JOURNAL      J. Immunol. 169 (8), 4437-4442 (2002)

PUBMED       [12370378](#)

REMARK      GenerIF: Following burn injury, liver mononuclear leukocytes--especially NK cells--produce a large amount of IFN-gamma in vitro without any additional stimulation.

REFERENCE    38 (bases 1 to 1208)

AUTHORS      Soutto,M., Zhang,F., Enerson,B., Tong,Y., Boothby,M. and Aune,T.M.

TITLE        A minimal IFN-gamma promoter confers Th1 selective expression

JOURNAL      J. Immunol. 169 (8), 4205-4212 (2002)

PUBMED       [12370350](#)

REMARK      GenerIF: A minimal IFN-gamma promoter contains a T box expressed in a T-bet responsive unit within the -565 to -410 region of the IFN-gamma promoter and is sufficient to confer Th1 selective expression upon a reporter.

REFERENCE    39 (bases 1 to 1208)

AUTHORS      Ghiasi,H., Osorio,Y., Hedvat,Y., Perng,G.C., Nesburn,A.B. and Wechsler,S.L.

TITLE        Infection of BALB/c mice with a herpes simplex virus type 1 recombinant virus expressing IFN-gamma driven by the LAT promoter

JOURNAL      Virology 302 (1), 144-154 (2002)

PUBMED       [12429523](#)

REMARK      GenerIF: role of interferon-gamma in Herpes Simplex Virus Type 1 protection

REFERENCE    40 (bases 1 to 1208)

AUTHORS      Toliver-Kinsky,T.E., Varma,T.K., Lin,C.Y., Herndon,D.N. and Sherwood,E.R.

TITLE        Interferon-gamma production is suppressed in thermally injured mice: decreased production of regulatory cytokines and corresponding receptors

JOURNAL      Shock 18 (4), 322-330 (2002)

PUBMED       [12392275](#)

REMARK      GenerIF: We conclude that burn-associated suppression of IFN-gamma is due to deficient production of inducing factors and their receptors, leading to severe impairments in cellular IFN-gamma induction pathways.

REFERENCE    41 (bases 1 to 1208)

AUTHORS      Refaeli,Y., Van Parijs,L., Alexander,S.I. and Abbas,A.K.

TITLE        Interferon gamma is required for activation-induced death of T lymphocytes

JOURNAL      J. Exp. Med. 196 (7), 999-1005 (2002)

PUBMED       [12370261](#)

REMARK      GenerIF: required for activation-induced death of T lymphocytes

- REFERENCE 42 (bases 1 to 1208)  
AUTHORS Yu, S., Sharp, G.C. and Braley-Mullen, H.  
TITLE Dual roles for IFN-gamma, but not for IL-4, in spontaneous autoimmune thyroiditis in NOD.H-2h4 mice  
JOURNAL J. Immunol. 169 (7), 3999-4007 (2002)  
PUBMED [12244202](#)  
REMARK GeneRIF: IFN-gamma is required for development of lymphocytic spontaneous autoimmune thyroiditis, and it also functions to inhibit thyroid epithelial cell proliferation.
- REFERENCE 43 (bases 1 to 1208)  
AUTHORS Plotnicky-Gilquin, H., Cyblat-Chanal, D., Aubry, J.P., Champion, T., Beck, A., Nguyen, T., Bonnefoy, J.Y. and Corvaia, N.  
TITLE Gamma interferon-dependent protection of the mouse upper respiratory tract following parenteral immunization with a respiratory syncytial virus G protein fragment  
JOURNAL J. Virol. 76 (20), 10203-10210 (2002)  
PUBMED [12239295](#)  
REMARK GeneRIF: T-helper-cell epitope of RSV G protein induces URT protection in mice after parenteral immunization through a Th1-type, IFN-gamma-dependent mechanism
- REFERENCE 44 (bases 1 to 1208)  
AUTHORS Metwali, A., Blum, A., Elliott, D.E. and Weinstock, J.V.  
TITLE Interleukin-4 receptor alpha chain and STAT6 signaling inhibit gamma interferon but not Th2 cytokine expression within schistosome granulomas  
JOURNAL Infect. Immun. 70 (10), 5651-5658 (2002)  
PUBMED [12228294](#)  
REMARK GeneRIF: Interleukin-4 receptor alpha chain and STAT6 signaling inhibit gamma interferon but not Th2 cytokine expression within schistosome granulomas.
- REFERENCE 45 (bases 1 to 1208)  
AUTHORS Espejo, C., Penkowa, M., Saez-Torres, I., Hidalgo, J., Garcia, A., Montalban, X. and Martinez-Caceres, E.M.  
TITLE Interferon-gamma regulates oxidative stress during experimental autoimmune encephalomyelitis  
JOURNAL Exp. Neurol. 177 (1), 21-31 (2002)  
PUBMED [12429207](#)  
REMARK GeneRIF: Interferon-gamma has a protective role against experimental autoimmune encephalomyelitis by regulating the level of oxidative stress.
- REFERENCE 46 (bases 1 to 1208)  
AUTHORS Hirota, R., Tajima, S., Yoneda, Y., Tamayama, T., Watanabe, M., Ueda, K., Kubota, T. and Yoshida, R.  
TITLE Alopecia of IFN-gamma knockout mouse as a model for disturbance of the hair cycle: a unique arrest of the hair cycle at the anagen phase accompanied by mitosis  
JOURNAL J. Interferon Cytokine Res. 22 (9), 935-945 (2002)  
PUBMED [12396715](#)  
REMARK GeneRIF: The lack of IFN-gamma around 3 weeks of age is directly responsible for alopecia due to a unique arrest of the hair cycle at the anagen phase accompanied by mitosis..
- REFERENCE 47 (bases 1 to 1208)  
AUTHORS Nguyen, K.B., Watford, W.T., Salomon, R., Hofmann, S.R., Pien, G.C., Morinobu, A., Gadina, M., O'Shea, J.J. and Biron, C.A.  
TITLE Critical role for STAT4 activation by type 1 interferons in the interferon-gamma response to viral infection  
JOURNAL Science 297 (5589), 2063-2066 (2002)  
PUBMED [12242445](#)  
REMARK GeneRIF: demonstrated that IFN-alpha activates STAT4 directly and that this is required for IFN-gamma production during viral

- infections of mice, in concert with T cell receptor-derived signals
- REFERENCE 48 (bases 1 to 1208)
- AUTHORS Morinobu,A., Gadina,M., Strober,W., Visconti,R., Fornace,A.,  
Montagna,C., Feldman,G.M., Nishikomori,R. and O'Shea,J.J.
- TITLE STAT4 serine phosphorylation is critical for IL-12-induced  
IFN-gamma production but not for cell proliferation
- JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (19), 12281-12286 (2002)
- PUBMED [12213961](#)
- REMARK GeneRIF: phosphorylation of STAT4 on both tyrosine and serine  
residues is important in promoting normal T(H)1 differentiation and  
IFN-gamma secretion
- REFERENCE 49 (bases 1 to 1208)
- AUTHORS Barton,L.F., Cruz,M., Rangwala,R., Deepe,G.S. Jr. and Monaco,J.J.
- TITLE Regulation of immunoproteasome subunit expression in vivo following  
pathogenic fungal infection
- JOURNAL J. Immunol. 169 (6), 3046-3052 (2002)
- PUBMED [12218120](#)
- REMARK GeneRIF: IFN-gamma is essential for up-regulation, but not  
constitutive expression, of immunoproteasome subunits.
- REFERENCE 50 (bases 1 to 1208)
- AUTHORS Sobek,V., Balkow,S., Korner,H. and Simon,M.M.
- TITLE Antigen-induced cell death of T effector cells in vitro proceeds  
via the Fas pathway, requires endogenous interferon-gamma and is  
independent of perforin and granzymes
- JOURNAL Eur. J. Immunol. 32 (9), 2490-2499 (2002)
- PUBMED [12207333](#)
- REMARK GeneRIF: Antigen-induced cell death of T effector cells in vitro  
requires endogenous interferon-gamma. The perforin plus  
granzyme-independent and FasL and/or TNF-alpha facilitated process  
of AgICD of T effector cells is tightly regulated by endogenous  
IFN-gamma.
- REFERENCE 51 (bases 1 to 1208)
- AUTHORS Romanha,A.J., Alves,R.O., Murta,S.M., Silva,J.S., Ropert,C. and  
Gazzinelli,R.T.
- TITLE Experimental chemotherapy against Trypanosoma cruzi infection:  
essential role of endogenous interferon-gamma in mediating  
parasitologic cure
- JOURNAL J. Infect. Dis. 186 (6), 823-828 (2002)
- PUBMED [12198617](#)
- REMARK GeneRIF: Experimental chemotherapy against Trypanosoma cruzi  
infection: essential role of endogenous interferon-gamma in  
mediating parasitologic cure
- REFERENCE 52 (bases 1 to 1208)
- AUTHORS John,B., Rajagopal,D., Pashine,A., Rath,S., George,A. and Bal,V.
- TITLE Role of IL-12-independent and IL-12-dependent pathways in  
regulating generation of the IFN-gamma component of T cell  
responses to Salmonella typhimurium
- JOURNAL J. Immunol. 169 (5), 2545-2552 (2002)
- PUBMED [12193724](#)
- REMARK GeneRIF: Rapid ingress of live Salmonella typhimurium into  
antigen-presenting cells and associated early antigen  
presentation-related events culminate in generation of the  
IFN-gamma-committed CD4 T cell component of the immune response in  
Salmonella infection.
- REFERENCE 53 (bases 1 to 1208)
- AUTHORS Steele,C., Zheng,M., Young,E., Marrero,L., Shellito,J.E. and  
Kolls,J.K.
- TITLE Increased host resistance against Pneumocystis carinii pneumonia in  
gammadelta T-cell-deficient mice: protective role of gamma  
interferon and CD8(+) T cells

JOURNAL Infect. Immun. 70 (9), 5208-5215 (2002)  
PUBMED [12183572](#)  
REMARK GenerIF: presence of gammadelta-TCR(+) T cells modulates host susceptibility to *P. carinii* pneumonia through interactions with pulmonary CD8(+) T cells and tissue production of IFN-gamma

REFERENCE 54 (bases 1 to 1208)  
AUTHORS Topisirovic, I., Capili, A.D. and Borden, K.L.  
TITLE Gamma interferon and cadmium treatments modulate eukaryotic initiation factor 4E-dependent mRNA transport of cyclin D1 in a PML-dependent manner

JOURNAL Mol. Cell. Biol. 22 (17), 6183-6198 (2002)  
PUBMED [12167712](#)  
REFERENCE 55 (bases 1 to 1208)  
AUTHORS Ishida, Y., Kondo, T., Ohshima, T., Fujiwara, H., Iwakura, Y. and Mukaida, N.  
TITLE A pivotal involvement of IFN-gamma in the pathogenesis of acetaminophen-induced acute liver injury

JOURNAL FASEB J. 16 (10), 1227-1236 (2002)  
PUBMED [12153990](#)  
REMARK GenerIF: involvement of IFN-gamma in the pathogenesis of acetaminophen-induced acute liver injury

REFERENCE 56 (bases 1 to 1208)  
AUTHORS Ellis, T.N. and Beaman, B.L.  
TITLE Murine polymorphonuclear neutrophils produce interferon-gamma in response to pulmonary infection with *Nocardia asteroides*

JOURNAL J. Leukoc. Biol. 72 (2), 373-381 (2002)  
PUBMED [12149429](#)  
REMARK GenerIF: This is the first report of IFN-gamma production by neutrophils in response to an infection in vivo, a murine model of *N. asteroides* pulmonary infection.

REFERENCE 57 (bases 1 to 1208)  
AUTHORS Gomez, M.I., Sordelli, D.O., Buzzola, F.R. and Garcia, V.E.  
TITLE Induction of cell-mediated immunity to *Staphylococcus aureus* in the mouse mammary gland by local immunization with a live attenuated mutant

JOURNAL Infect. Immun. 70 (8), 4254-4260 (2002)  
PUBMED [12117934](#)  
REMARK GenerIF: INF-gamma production induced by intramammary immunization may play a pivotal role in the eradication of intracellular staphylococci

REFERENCE 58 (bases 1 to 1208)  
AUTHORS Hixon, J.A., Anver, M.R., Blazar, B.R., Panoskaltsis-Mortari, A., Wiltrot, R.H. and Murphy, W.J.  
TITLE Administration of either anti-CD40 or interleukin-12 following lethal total body irradiation induces acute lethal toxicity affecting the gut

JOURNAL Biol Blood Marrow Transplant 8 (6), 316-325 (2002)  
PUBMED [12108917](#)  
REMARK GenerIF: role of IFN-gamma in IL-12-mediated toxicity

REFERENCE 59 (bases 1 to 1208)  
AUTHORS Hu, J., Meng, Q., Roy, S.K., Raha, A., Hu, J., Zhang, J., Hashimoto, K. and Kalvakolanu, D.V.  
TITLE A novel transactivating factor that regulates interferon-gamma-dependent gene expression

JOURNAL J. Biol. Chem. 277 (33), 30253-30263 (2002)  
PUBMED [12050152](#)  
REFERENCE 60 (bases 1 to 1208)  
AUTHORS Freudenberg, M.A., Merlin, T., Kalis, C., Chvatchko, Y., Stubig, H. and Galanos, C.  
TITLE Cutting edge: a murine, IL-12-independent pathway of IFN-gamma

induction by gram-negative bacteria based on STAT4 activation by Type I IFN and IL-18 signaling

JOURNAL J. Immunol. 169 (4), 1665-1668 (2002)  
PUBMED [12165484](#)  
REMARK GeneRIF: IFN- $\alpha$ beta-dependent pathway of IFN- $\gamma$  induction in mice.

REFERENCE 61 (bases 1 to 1208)  
AUTHORS Carvalho-Pinto,C.E., Garcia,M.I., Mellado,M., Rodriguez-Frade,J.M., Martin-Caballero,J., Flores,J., Martinez-A,C. and Balomenos,D.  
TITLE Autocrine production of IFN- $\gamma$  by macrophages controls their recruitment to kidney and the development of glomerulonephritis in MRL/lpr mice  
JOURNAL J. Immunol. 169 (2), 1058-1067 (2002)  
PUBMED [12097414](#)  
REMARK GeneRIF: IFN- $\gamma$  production by infiltrating macrophages, and not by T cells, is responsible for adhesion molecule up-regulation, macrophage accumulation, and inflammation in MRL/lpr kidney, even in the absence of glomerular autoantibody deposits.

REFERENCE 62 (bases 1 to 1208)  
AUTHORS Fields,P.E., Kim,S.T. and Flavell,R.A.  
TITLE Cutting edge: changes in histone acetylation at the IL-4 and IFN- $\gamma$  loci accompany Th1/Th2 differentiation  
JOURNAL J. Immunol. 169 (2), 647-650 (2002)  
PUBMED [12097365](#)  
REMARK GeneRIF: Profound increases in histone acetylation occur at the IFN- $\gamma$  locus during Th1/Th2 cell differentiation.

REFERENCE 63 (bases 1 to 1208)  
AUTHORS Hosohara,K., Ueda,H., Kashiwamura,S., Yano,T., Ogura,T., Marukawa,S. and Okamura,H.  
TITLE Interleukin-18 induces acute biphasic reduction in the levels of circulating leukocytes in mice  
JOURNAL Clin. Diagn. Lab. Immunol. 9 (4), 777-783 (2002)  
PUBMED [12093672](#)  
REMARK GeneRIF: IL18 induced acute biphasic reduction in the levels of circulating leukocytes is mediated by NO and IFN- $\gamma$ .

REFERENCE 64 (bases 1 to 1208)  
AUTHORS Vandebroek,K., Alloza,I., Brehmer,D., Billiau,A., Proost,P., McFerran,N., Rudiger,S. and Walker,B.  
TITLE The conserved helix C region in the superfamily of interferon- $\gamma$  /interleukin-10-related cytokines corresponds to a high-affinity binding site for the HSP70 chaperone DnaK  
JOURNAL J. Biol. Chem. 277 (28), 25668-25676 (2002)  
PUBMED [11970958](#)  
REMARK GeneRIF: conserved helix C region in the superfamily of interferon- $\gamma$  /interleukin-10-related cytokines corresponds to a high-affinity binding site for the HSP70 chaperone DnaK

REFERENCE 65 (bases 1 to 1208)  
AUTHORS Kamperschroer,C. and Quinn,D.G.  
TITLE The role of proinflammatory cytokines in wasting disease during lymphocytic choriomeningitis virus infection  
JOURNAL J. Immunol. 169 (1), 340-349 (2002)  
PUBMED [12077263](#)  
REMARK GeneRIF: Proinflammatory IFN- $\gamma$  is necessary for viral-specific CD4 T cell responses in the central nervous system during development of lymphocytic choriomeningitis virus-induced wasting disease.

REFERENCE 66 (bases 1 to 1208)  
AUTHORS Mullbacher,A., Lobigs,M., Hla,R.T., Tran,T., Stehle,T. and Simon,M.M.  
TITLE Antigen-dependent release of IFN- $\gamma$  by cytotoxic T cells



- up-regulates Fas on target cells and facilitates exocytosis-independent specific target cell lysis
- JOURNAL J. Immunol. 169 (1), 145-150 (2002)  
PUBMED [12077239](#)  
REMARK GeneRIF: IFN-gamma is the principal mediator responsible for cytolytic T effector cell-mediated up-regulation of Fas on target cells and enhancement of exocytosis-independent specific target cell lysis.
- REFERENCE 67 (bases 1 to 1208)  
AUTHORS Minami,M., Kita,M., Yan,X.Q., Yamamoto,T., Iida,T., Sekikawa,K., Iwakura,Y. and Imanishi,J.  
TITLE Role of IFN-gamma and tumor necrosis factor-alpha in herpes simplex virus type 1 infection  
JOURNAL J. Interferon Cytokine Res. 22 (6), 671-676 (2002)  
PUBMED [12162877](#)  
REMARK GeneRIF: results suggest that IFN-gamma and TNF-alpha play an important role in acute herpes simplex virus type 1 infection and reactivation from latency
- REFERENCE 68 (bases 1 to 1208)  
AUTHORS Gray,C.A. and Lawrence,R.A.  
TITLE Interferon-gamma and nitric oxide production are not required for the immune-mediated clearance of Brugia malayi microfilariae in mice  
JOURNAL Parasite Immunol. 24 (6), 329-336 (2002)  
PUBMED [12102718](#)  
REMARK GeneRIF: Interferon-gamma is not required for the immune-mediated clearance of Brugia malayi microfilariae in mice
- REFERENCE 69 (bases 1 to 1208)  
AUTHORS Calorini,L., Bianchini,F., Mannini,A., Mugnai,G., Balzi,M., Becciolini,A. and Ruggieri,S.  
TITLE IFNgamma and TNFalpha account for a pro-clonogenic activity secreted by activated murine peritoneal macrophages  
JOURNAL Clin. Exp. Metastasis 19 (3), 259-264 (2002)  
PUBMED [12067206](#)  
REMARK GeneRIF: IFNgamma and TNFalpha account for a pro-clonogenic activity secreted by activated murine peritoneal macrophages
- REFERENCE 70 (bases 1 to 1208)  
AUTHORS Yi,S. and O'Connell,P.J.  
TITLE IFN-gamma but not IL-4 is important for mouse CD4+ T cell-mediated macrophage activation following their exposure to pig cells in vitro  
JOURNAL Xenotransplantation 9 (4), 268-276 (2002)  
PUBMED [12060463](#)  
REMARK GeneRIF: important for mouse CD4+ T cell-mediated macrophage activation following their exposure to pig cells in vitro
- REFERENCE 71 (bases 1 to 1208)  
AUTHORS Smeltz,R.B., Chen,J., Ehrhardt,R. and Shevach,E.M.  
TITLE Role of IFN-gamma in Th1 differentiation: IFN-gamma regulates IL-18R alpha expression by preventing the negative effects of IL-4 and by inducing/maintaining IL-12 receptor beta 2 expression  
JOURNAL J. Immunol. 168 (12), 6165-6172 (2002)  
PUBMED [12055229](#)  
REMARK GeneRIF: IFN-gamma has pleiotropic effects in the regulation of IL-12 receptor beta 2 and IL-18 receptor alpha expression and function, and thus control of IL-12-dependent and IL-12-independent Th1 cell differentiation.
- REFERENCE 72 (bases 1 to 1208)  
AUTHORS Roy,S.K., Hu,J., Meng,Q., Xia,Y., Shapiro,P.S., Reddy,S.P., Platanias,L.C., Lindner,D.J., Johnson,P.F., Pritchard,C., Pages,G., Pouyssegur,J. and Kalvakolanu,D.V.

TITLE MEKK1 plays a critical role in activating the transcription factor C/EBP-beta-dependent gene expression in response to IFN-gamma  
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (12), 7945-7950 (2002)  
PUBMED [12048245](#)  
REMARK GeneRIF: MEKK1 plays a critical role in activating the transcription factor C/EBP-beta-dependent gene expression in response to IFN-gamma.

REFERENCE 73 (bases 1 to 1208)  
AUTHORS Kelso,A., Costelloe,E.O., Johnson,B.J., Groves,P., Buttigieg,K. and Fitzpatrick,D.R.  
TITLE The genes for perforin, granzymes A-C and IFN-gamma are differentially expressed in single CD8(+) T cells during primary activation  
JOURNAL Int. Immunol. 14 (6), 605-613 (2002)  
PUBMED [12039912](#)  
REMARK GeneRIF: the genes for perforin, the three major T cell granzymes (A-C) and IFN-gamma are differentially expressed during primary activation of naive CD8(+) T cells, kinetically and at the single-cell level

REFERENCE 74 (bases 1 to 1208)  
AUTHORS Obonyo,M., Guiney,D.G., Harwood,J., Fierer,J. and Cole,S.P.  
TITLE Role of gamma interferon in Helicobacter pylori induction of inflammatory mediators during murine infection  
JOURNAL Infect. Immun. 70 (6), 3295-3299 (2002)  
PUBMED [12011029](#)  
REMARK GeneRIF: INF-gamma mediates the induction of MIP-2 and iNOS mRNA expression by H. pylori in mice.

REFERENCE 75 (bases 1 to 1208)  
AUTHORS Abbas,N., Bednar,I., Mix,E., Marie,S., Paterson,D., Ljungberg,A., Morris,C., Winblad,B., Nordberg,A. and Zhu,J.  
TITLE Up-regulation of the inflammatory cytokines IFN-gamma and IL-12 and down-regulation of IL-4 in cerebral cortex regions of APP(SWE) transgenic mice  
JOURNAL J. Neuroimmunol. 126 (1-2), 50-57 (2002)  
PUBMED [12020956](#)  
REMARK GeneRIF: These results suggest a major pro-inflammatory role for IL-12 and IFN-gamma in Tg2576 transgenic mice that may provide the association between beta-amyloid plaque formation and microglial and astrocyte activation in these animals.

REFERENCE 76 (bases 1 to 1208)  
AUTHORS Khaskhely,N.M., Maruno,M., Uezato,H., Takamiyagi,A., Ramzi,S.T., Al-Kasem,K.M., Kariya,K., Toda,T., Hashiguchi,Y., Gomez Landires,E.A. and Nonaka,S.  
TITLE Low-dose UVB contributes to host resistance against Leishmania amazonensis infection in mice through induction of gamma interferon and tumor necrosis factor alpha cytokines  
JOURNAL Clin. Diagn. Lab. Immunol. 9 (3), 677-686 (2002)  
PUBMED [11986277](#)  
REMARK GeneRIF: low-dose UVB irradiation played a pathogen-suppressing role in Leishmania-susceptible BALB/c mice via systemic and local upregulation of Th1 (IFN-gamma and TNF-alpha) cytokines

REFERENCE 77 (bases 1 to 1208)  
AUTHORS Varma,T.K., Lin,C.Y., Toliver-Kinsky,T.E. and Sherwood,E.R.  
TITLE Endotoxin-induced gamma interferon production: contributing cell types and key regulatory factors  
JOURNAL Clin. Diagn. Lab. Immunol. 9 (3), 530-543 (2002)  
PUBMED [11986256](#)  
REMARK GeneRIF: data demonstrate that IL-10 and IL-12 are key functional regulators of LPS-induced IFN-gamma production

REFERENCE 78 (bases 1 to 1208)

AUTHORS Rodriguez,F., Harkins,S., Slifka,M.K. and Whitton,J.L.  
TITLE Immunodominance in virus-induced CD8(+) T-cell responses is dramatically modified by DNA immunization and is regulated by gamma interferon  
JOURNAL J. Virol. 76 (9), 4251-4259 (2002)  
PUBMED 11932390  
REMARK GeneRIF: regulates immunodominance in virus-induced CD8-positive t-lymphocyte responses  
REFERENCE 79 (bases 1 to 1208)  
AUTHORS Rais,M., Wild,J.S., Choudhury,B.K., Alam,R., Stafford,S., Dharajiya,N. and Sur,S.  
TITLE Interleukin-12 inhibits eosinophil differentiation from bone marrow stem cells in an interferon-gamma-dependent manner in a mouse model of asthma  
JOURNAL Clin. Exp. Allergy 32 (4), 627-632 (2002)  
PUBMED 11972612  
REMARK GeneRIF: Interleukin-12 inhibition of eosinophil differentiation from bone marrow stem cells is interferon-gamma-dependent in a mouse model of asthma.  
REFERENCE 80 (bases 1 to 1208)  
AUTHORS Dorner,B.G., Scheffold,A., Rolph,M.S., Huser,M.B., Kaufmann,S.H., Radbruch,A., Flesch,I.E. and Kroccek,R.A.  
TITLE MIP-1alpha, MIP-1beta, RANTES, and ATAC/lymphotactin function together with IFN-gamma as type 1 cytokines  
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (9), 6181-6186 (2002)  
PUBMED 11972057  
REMARK GeneRIF: MIP-1alpha, MIP-1beta, RANTES, and ATAC/lymphotactin function together with IFN-gamma as type 1 cytokines.  
REFERENCE 81 (bases 1 to 1208)  
AUTHORS Timoshanko,J.R., Holdsworth,S.R., Kitching,A.R. and Tipping,P.G.  
TITLE IFN-gamma production by intrinsic renal cells and bone marrow-derived cells is required for full expression of crescentic glomerulonephritis in mice  
JOURNAL J. Immunol. 168 (8), 4135-4141 (2002)  
PUBMED 11937574  
REMARK GeneRIF: IFN-gamma production by both bone marrow-derived cells and intrinsic renal cells is required for the full expression of crescentic glomerulonephritis and for the development of delayed-type hypersensitivity in kidney and skin.  
REFERENCE 82 (bases 1 to 1208)  
AUTHORS Flaishon,L., Topilski,I., Shoseyov,D., HersHKoviz,R., Fireman,E., Levo,Y., Marmor,S. and Shachar,I.  
TITLE Cutting edge: anti-inflammatory properties of low levels of IFN-gamma  
JOURNAL J. Immunol. 168 (8), 3707-3711 (2002)  
PUBMED 11937520  
REMARK GeneRIF: Low dose IFN-gamma appears to exert global suppressive effects on T cell trafficking and may have clinical application as an anti-inflammatory agent.  
REFERENCE 83 (bases 1 to 1208)  
AUTHORS Kohda,C., Kawamura,I., Baba,H., Nomura,T., Ito,Y., Kimoto,T., Watanabe,I. and Mitsuyama,M.  
TITLE Dissociated linkage of cytokine-inducing activity and cytotoxicity to different domains of listeriolysin O from Listeria monocytogenes  
JOURNAL Infect. Immun. 70 (3), 1334-1341 (2002)  
PUBMED 11854218  
REMARK GeneRIF: Listeriolysin induces interferon production by spleen cells.  
REFERENCE 84 (bases 1 to 1208)  
AUTHORS Nomura,T., Kawamura,I., Tsuchiya,K., Kohda,C., Baba,H., Ito,Y.,

Kimoto,T., Watanabe,I. and Mitsuyama,M.  
TITLE Essential role of interleukin-12 (IL-12) and IL-18 for gamma  
interferon production induced by listeriolysin O in mouse spleen  
cells  
JOURNAL Infect. Immun. 70 (3), 1049-1055 (2002)  
PUBMED [11854182](#)  
REMARK GenerIF: LLO, a well-known virulence factor of *L. monocytogenes*, is  
capable of inducing IFN-gamma from NK cells through induction of  
IL-12 and IL-18 from macrophages.  
REFERENCE 85 (bases 1 to 1208)  
AUTHORS Smyth,M.J., Crowe,N.Y., Pellicci,D.G., Kyparissoudis,K.,  
Kelly,J.M., Takeda,K., Yagita,H. and Godfrey,D.I.  
TITLE Sequential production of interferon-gamma by NK1.1(+) T cells and  
natural killer cells is essential for the antimetastatic effect of  
alpha-galactosylceramide  
JOURNAL Blood 99 (4), 1259-1266 (2002)  
PUBMED [11830474](#)  
REMARK GenerIF: essential for the antimetastatic effect of  
alpha-galactosylceramide  
REFERENCE 86 (bases 1 to 1208)  
AUTHORS Skoberne,M. and Geginat,G.  
TITLE Efficient in vivo presentation of *Listeria monocytogenes*- derived  
CD4 and CD8 T cell epitopes in the absence of IFN-gamma  
JOURNAL J. Immunol. 168 (4), 1854-1860 (2002)  
PUBMED [11823519](#)  
REMARK GenerIF: Interferon-gamma is not required for antigen presentation  
of *Listeria monocytogenes* epitopes  
REFERENCE 87 (bases 1 to 1208)  
AUTHORS Shimozato,O., Ortaldo,J.R., Komschlies,K.L. and Young,H.A.  
TITLE Impaired NK cell development in an IFN-gamma transgenic mouse:  
aberrantly expressed IFN-gamma enhances hematopoietic stem cell  
apoptosis and affects NK cell differentiation  
JOURNAL J. Immunol. 168 (4), 1746-1752 (2002)  
PUBMED [11823506](#)  
REMARK GenerIF: interferon-gamma transgenic mice have enhanced  
hematopoietic stem cell apoptosis and NK cell differentiation is  
altered  
REFERENCE 88 (bases 1 to 1208)  
AUTHORS Schloot,N.C., Hanifi-Moghaddam,P., Goebel,C., Shatavi,S.V.,  
Flohe,S., Kolb,H. and Rothe,H.  
TITLE Serum IFN-gamma and IL-10 levels are associated with disease  
progression in non-obese diabetic mice  
JOURNAL Diabetes Metab Res Rev 18 (1), 64-70 (2002)  
PUBMED [11921420](#)  
REMARK GenerIF: the ratio of IFN-gamma/IL-10 in the serum was  
significantly increased in diabetic compared to non-diabetic NOD  
mice  
REFERENCE 89 (bases 1 to 1208)  
AUTHORS Metcalf,D., Mifsud,S., Di Rago,L., Nicola,N.A., Hilton,D.J. and  
Alexander,W.S.  
TITLE Polycystic kidneys and chronic inflammatory lesions are the delayed  
consequences of loss of the suppressor of cytokine signaling-1  
(SOCS-1)  
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (2), 943-948 (2002)  
PUBMED [11782537](#)  
REMARK GenerIF: Mice with inactivation of the gene encoding the suppressor  
of cytokine signaling-1 (SOCS-1) die in neonatal life with an  
IFN-gamma-dependent inflammatory disease dominated by fatty  
degeneration and necrosis of the liver.  
REFERENCE 90 (bases 1 to 1208)

AUTHORS Szabo,S.J., Sullivan,B.M., Stemmann,C., Satoskar,A.R.,  
Sleckman,B.P. and Glimcher,L.H.

TITLE Distinct effects of T-bet in Th1 lineage commitment and IFN-gamma  
production in CD4 and CD8 T cells

JOURNAL Science 295 (5553), 338-342 (2002)

PUBMED [11786644](#)

REMARK GeneRIF: regulation of IFN-gamma is controlled by distinct  
transcriptional mechanisms within the T cell lineage

REFERENCE 91

AUTHORS The FANTOM Consortium and the RIKEN Genome Exploration Research  
Group Phase I & II Team.

TITLE Analysis of the mouse transcriptome based on functional annotation  
of 60,770 full-length cDNAs

JOURNAL Nature 420, 563-573 (2002)

REFERENCE 92 (bases 1 to 1208)

AUTHORS Savinov,A.Y., Wong,F.S. and Chervonsky,A.V.

TITLE IFN-gamma affects homing of diabetogenic T cells

JOURNAL J. Immunol. 167 (11), 6637-6643 (2001)

PUBMED [11714835](#)

REMARK GeneRIF: IFN-gamma contributes to the development of autoimmune  
diabetes by regulating the penetration of the pancreatic islets by  
diabetogenic T cells.

REFERENCE 93 (bases 1 to 1208)

AUTHORS Rothfuchs,A.G., Gigliotti,D., Palmblad,K., Andersson,U., Wigzell,H.  
and Rottenberg,M.E.

TITLE IFN-alpha beta-dependent, IFN-gamma secretion by bone  
marrow-derived macrophages controls an intracellular bacterial  
infection

JOURNAL J. Immunol. 167 (11), 6453-6461 (2001)

PUBMED [11714812](#)

REMARK GeneRIF: IFN-gamma secretion induced by Chlamydia pneumoniae  
infection in bone marrow-derived macrophages mediates control of  
the infecting bacteria by an intracellular autocrine/paracrine loop  
mechanism.

REFERENCE 94 (bases 1 to 1208)

AUTHORS Ben Jilani,K.E., Akarid,K., Arnoult,D., Petit,F., Baert,E.,  
Gaillard,J.P., Ameisen,J.C. and Estaquier,J.

TITLE Gamma-interferon induces apoptosis of the B lymphoma WEHI-279 cell  
line through a CD95/CD95L-independent mechanism

JOURNAL Eur. Cytokine Netw. 12 (4), 587-596 (2001)

PUBMED [11781185](#)

REMARK GeneRIF: role in regulating B cell apoptosis

REFERENCE 95 (bases 1 to 1208)

AUTHORS Cochrane,R., Clark,R.B., Huang,C.K. and Cone,R.E.

TITLE Differential regulation of T cell receptor-mediated Th1 cell  
IFN-gamma production and proliferation by divergent cAMP-mediated  
redox pathways

JOURNAL J. Interferon Cytokine Res. 21 (10), 797-807 (2001)

PUBMED [11710991](#)

REMARK GeneRIF: regulation of Th1 cell IFN-gamma production by  
cAMP-mediated redox pathways

REFERENCE 96 (bases 1 to 1208)

AUTHORS Das,G., Sheridan,S. and Janeway,C.A. Jr.

TITLE The source of early IFN-gamma that plays a role in Th1 priming

JOURNAL J. Immunol. 167 (4), 2004-2010 (2001)

PUBMED [11489982](#)

REMARK GeneRIF: The initial burst of IFN-gamma that primes Th1 cells is  
produced by an MHC class Ib, TAP-independent subset of CD8 T cells.

REFERENCE 97 (bases 1 to 1208)

AUTHORS Furlan,R., Brambilla,E., Ruffini,F., Poliani,P.L., Bergami,A.,

Marconi,P.C., Franciotta,D.M., Penna,G., Comi,G., Adorini,L. and Martino,G.

TITLE Intrathecal delivery of IFN-gamma protects C57BL/6 mice from chronic-progressive experimental autoimmune encephalomyelitis by increasing apoptosis of central nervous system-infiltrating lymphocytes

JOURNAL J. Immunol. 167 (3), 1821-1829 (2001)

PUBMED [11466408](#)

REMARK GeneRIF: Central nervous system-specific production of IFN-gamma can protect mice from progression of autoimmune demyelination by inducing rapid clearance of encephalitogenic T cells infiltrating the CNS parenchyma via an apoptotic pathway.

REFERENCE 98 (bases 1 to 1208)

AUTHORS Ford,J.G., Rennick,D., Donaldson,D.D., Venkayya,R., McArthur,C., Hansell,E., Kurup,V.P., Warnock,M. and Grunig,G.

TITLE IL-13 and IFN-gamma: interactions in lung inflammation

JOURNAL J. Immunol. 167 (3), 1769-1777 (2001)

PUBMED [11466402](#)

REMARK GeneRIF: In a model of experimental lung injury induced by mixed T cell responses, IFN-gamma (a Th1-cell mediator) simultaneously inhibited and potentiated the inflammatory effects induced by IL-13 (a Th2-cell mediator).

REFERENCE 99 (bases 1 to 1208)

AUTHORS Nakahira,M., Tomura,M., Iwasaki,M., Ahn,H.J., Bian,Y., Hamaoka,T., Ohta,T., Kurimoto,M. and Fujiwara,H.

TITLE An absolute requirement for STAT4 and a role for IFN-gamma as an amplifying factor in IL-12 induction of the functional IL-18 receptor complex

JOURNAL J. Immunol. 167 (3), 1306-1312 (2001)

PUBMED [11466347](#)

REMARK GeneRIF: IFN-gamma functions as an amplifying factor in IL-12 induction of the functional IL-18 receptor complex.

REFERENCE 100 (bases 1 to 1208)

AUTHORS Dijkmans,R., Volckaert,G., Van Damme,J., De Ley,M., Billiau,A. and De Somer,P.

TITLE Molecular cloning of murine interferon gamma (MuIFN-gamma) cDNA and its expression in heterologous mammalian cells

JOURNAL J. Interferon Res. 5 (3), 511-520 (1985)

PUBMED [2997340](#)

REFERENCE 101 (bases 1 to 1208)

AUTHORS Gray,P.W. and Goeddel,D.V.

TITLE Cloning and expression of murine immune interferon cDNA

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 80 (19), 5842-5846 (1983)

PUBMED [6310596](#)

COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final NCBI review. The reference sequence was derived from [AK089574.1](#).

FEATURES

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